

Primary Myoepithelioma of the Testis – A Case Report –

Seong Muk Jeong¹ · Jung Hee Lee¹
Won Young Park¹ · Na Ri Shin¹
Woo Gyeong Kim¹ · Gi Yeong Huh^{1,3}
Chang Hun Lee^{1,3} · Hong Koo Ha²

Departments of ¹Pathology and ²Urology,
³Medical Research Institute, Pusan National
University School of Medicine, Busan, Korea

Received: February 11, 2010

Accepted: April 26, 2010

Corresponding Author

Chang Hun Lee, M.D.
Department of Pathology, Pusan National University
Hospital, 1-10 Ami-dong, Seo-gu, Busan 602-739,
Korea
Tel: +82-51-240-7718
Fax: +82-51-242-7422
E-mail: cnlee@pusan.ac.kr

*This work was supported for two years by Pusan
National University.

Myoepitheliomas are well-established to occur in the salivary glands, but they have also been described in the breast, upper aerodigestive tract, skin, and soft tissues. We report here on a unique case of primary myoepithelioma that occurred in the right testis of a 28-year-old man. The tumor was entirely confined to the testis and it was clearly separated from the epididymis. Histopathology revealed mixed architectural patterns in which the reticular areas merged into the chondromyxoid stroma. The tumor cells, which were focally immunoreactive to pancytokeratin and S-100 protein, were round to ovoid and spindly arranged in cords, strands, and fascicles. They showed mild nuclear pleomorphism, sparse mitotic figures and a low Ki-67 proliferative index. There was no ductal differentiation in the tumor. To the best of our knowledge, there has been only one case report of a primary testicular myoepithelioma in the English medical literature.

Key Words: Myoepithelioma; Testis

Myoepitheliomas are now known as neoplasms that are entirely composed of myoepithelial cells with solid, myxoid, and/or reticular growth patterns. Although they occurs most commonly in the salivary glands, primary myoepithelioma has on rare occasion been described in the breast, upper aerodigestive tract, skin and soft tissues.¹⁻³ Perhaps due to their morphologic and immunophenotypic heterogeneity, these tumors are known to be poorly recognized and they may be mistaken for other soft tissue/stromal tumors when arising outside of the salivary glands. We report here on an exceptional case of primary myoepithelioma occurred in the right testis of a 28-year-old man. In the present case, the histologic findings and immunohistochemical results were characteristic of soft tissue myoepithelioma that has occurred in more commonly described locations.³ To the best of our knowledge, this is the second reported case of a primary testicular myoepithelioma in the English medical literature.

CASE REPORT

In June 2009, a 28-year-old man was referred to our hospital for evaluation of a painless solid mass in the right testis. A physical examination by a urologist revealed a firm testicular mass in the enlarged right testis. The magnetic resonance imaging scan showed a well-circumscribed heterogeneous mass measuring about 3.5 cm in the right testis (Fig. 1). The mass appeared to be well-confined within the testis and there is no evidence of significant lymphadenopathy in the inguinal and retroperitoneal sites. A urologic surgeon performed a radical orchiectomy via an inguinal incision. The pathologic diagnosis of myoepithelioma was made. At 1-year follow up without additional treatment, no evidence of local recurrence or metastasis was detected.

The surgical specimen showed a well circumscribed encapsulated mass that measured 3.5×3.2 cm. The cut surface was a solid gray to white mass with foci of hemorrhage and myxoid areas (Fig. 2). Microscopically, the tumor was well circumscribed by a fibrous capsule without evidence of infiltration into the

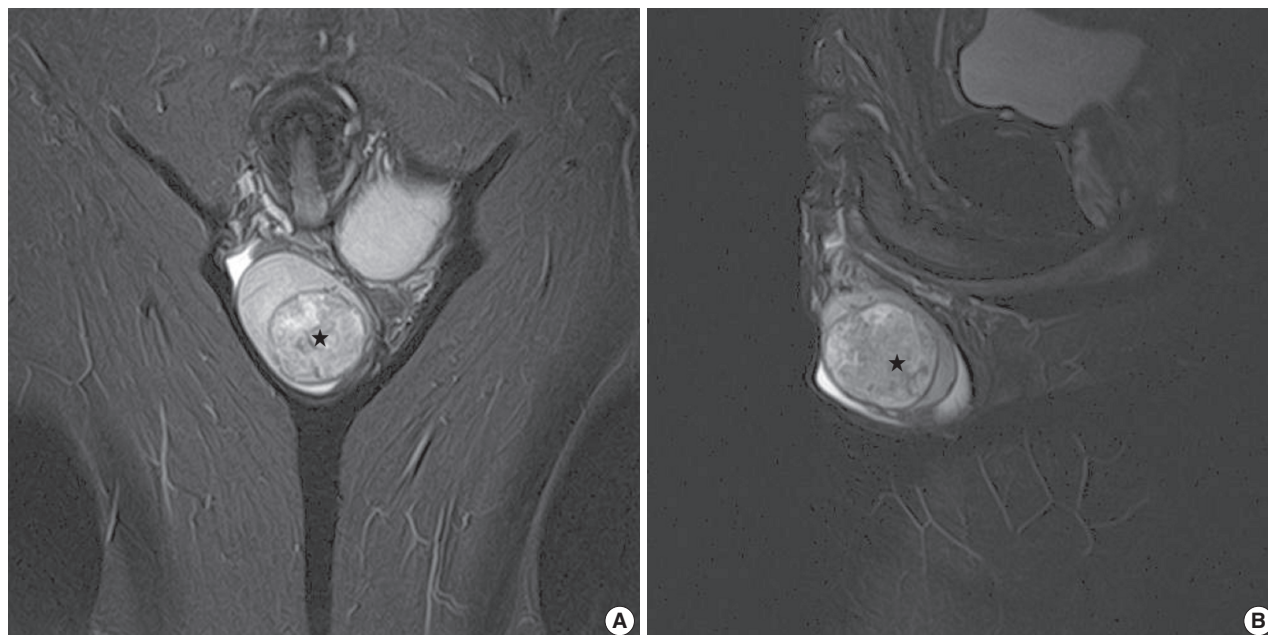


Fig. 1. (A, B) The magnetic resonance imaging scan reveals a well circumscribed solid mass (★) in the testis (A, coronal view; B, sagittal view).

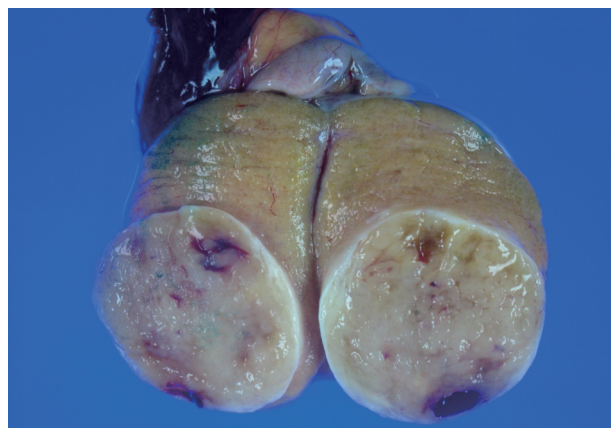


Fig. 2. A well circumscribed encapsulated solid mass of the right testis, with foci of hemorrhage and myxoid areas.

surrounding tissues (Fig. 3A). The tumor cells revealed mixed architectural patterns in which the reticular areas merged into the chondromyxoid stroma. Most of the tumor cells had round or spindled shaped nuclei with abundant eosinophilic cytoplasm (Fig. 3B). Focally, some large epithelioid cells displayed abundant vacuolated cytoplasm. The tumor cells had neither pleomorphism nor mitotic figures. Immunohistochemically, the tumor cells are strongly positive for vimentin and focally positive for pancytokeratin (Fig. 3C) and S-100 protein (Fig. 3D). However, they were negative for epithelial membrane antigen (EMA), CD117/c-kit, α -smooth muscle actin (SMA), p63, glial fibril-

lary acidic protein (GFAP), CD34 and inhibin- α . The Ki-67 proliferative index of the tumor cells was about 1% (Table 1). On the basis of the morphologic and immunohistochemical findings, the pathologic diagnosis of myoepithelioma was made.

DISCUSSION

Myoepithelioma is a benign tumor that is exclusively or almost exclusively composed of neoplastic cells that exhibit myoepithelial differentiation. The uncommon diagnosis of myoepithelioma in salivary glands was initially reserved for those tumors composed of spindle cells or plasmacytoid cells and that demonstrate a solid growth pattern. However, this category has recently been expanded to include those tumors with myxoid or hyalinized stroma, reticular or trabecular architecture, and epithelioid or clear myoepithelial cells.³ Similar criteria can be also applied for making the diagnosis of soft tissue myoepithelioma. On the contrary, mixed tumors are literally well circumscribed lesions displaying epithelial and/or myoepithelial elements, in varying proportions, within a hyalinized to chondromyxoid stroma. While some investigators have required the total absence of a ductal component for making the diagnosis of myoepithelioma,⁴ most accept the presence of a minor epithelial component (e.g., less than 5-10%).⁵⁻⁷ The present case did not reveal any definite ductal differentiation.

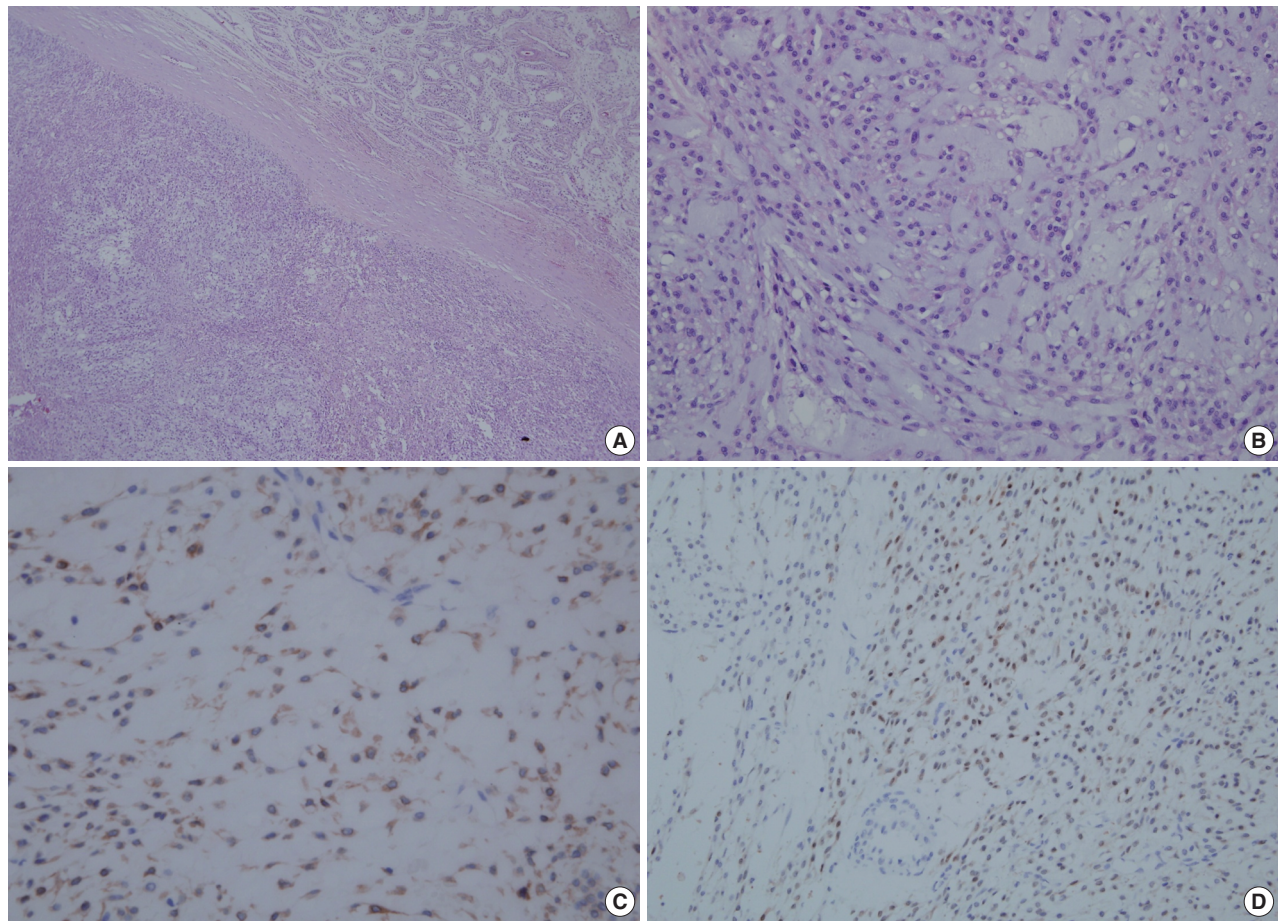


Fig. 3. The representative morphologic and immunohistochemical features of myoepithelioma in the right testis. (A) The tumor is well circumscribed by a fibrous capsule without evidence of focal infiltration into the surrounding tissues. (B) The tumor cells reveal a reticular pattern with chondromyxoid stroma and most of the tumor cells have round or spindly nuclei with abundant eosinophilic cytoplasm. (C) The cytoplasm of the tumor cells is positive for pancytokeratin. (D) The nuclei of the tumor cells are positive for S-100 protein.

Table 1. Results of immunohistochemical staining used in the present case

Antibody	Clone	Source	Result
Pan-cytokeratin	AE1/AE3	Biogenex	Focally positive
EMA	E29	Dako	Negative
Vimentin	V9	Zymed	Diffusely positive
Desmin	D33	Dako	Negative
α -SMA	1A4	Dako	Negative
GFAP	6F2	Dako	Negative
Inhibin- α	R1	Dako	Negative
p63	4A4	Neomarkers	Negative
c-kit	Polyclonal	Dako	Negative
S-100	Polyclonal	Novocastra	Focally positive
CD56	1B6	Novocastra	Negative
CD34	QBEnd-10	Dako	Negative

EMA, epithelial membrane antigen; α -SMA, α -smooth muscle actin; GFAP, glial fibrillary acidic protein.

Myoepithelial cells are ectodermally-derived contractile cells that are routinely identified in many normal tissues with secre-

tory function, such as the major and minor salivary glands, the lacrimal glands, sweat glands, breast, and the prostate.^{8,9} They originate from the same progenitor of epithelial cells, and they acquire the features of smooth muscle differentiation while retaining epithelial properties. In contrast to breast, sweat glands and salivary glands, where myoepithelial cells are abundant, the testes do not normally have myoepithelial cells.¹⁰ Instead, the testicular stroma includes peritubular myoid cells that consist of some scattered smooth muscle cells, myofibroblasts and CD-34-positive stromal cells. The tunica albuginea and the inner layer of the seminiferous tubules in adult testis are predominantly composed of myofibroblasts. Smooth muscle cells are also scattered throughout these sites in some cases. CD34-positive stromal cells are abundant and they form a reticular network around the seminiferous tubules and Leydig cells as well as the outer layer of the seminiferous tubules.¹¹ Regarding cytokeratin immunoreactivity in normal testis, rete testis epithelial

cells contain true desmosomes and tonofilaments and these cells show cytokeratin immunoreactivity. Weidner¹² reported on a spindle cell testicular tumor that showed both epithelial-like and myoid differentiation, and so it resembled myoepitheliomas of the skin, breast, and salivary gland. With performing ultrastructural and immunohistochemical studies, he suggested that the combined patterns in the testicular tumor may reflect peritubular myoid cell differentiation mixed with possible rete testis epithelial cell differentiation, although the presence of this peculiar tumor within the testis is difficult to explain. The present case exhibited the dual immunohistochemical pattern of epithelial and myoepithelial (not myogenous) differentiation, but peritubular myoid cell differentiation was not identified. Further, it is unfortunate that we could not perform electron microscopic study for our case. Before Weidner's report, Mietinen *et al.*¹³ described a testicular stromal tumor with epithelial differentiation, as was shown by ultrastructural, immunofluorescent and Western blot studies. We assume that their tumor may have been more brothersome than our case morphologically and immunophenotypically, although they did not mention the term 'myoepithelioma.' Anyway, it is perplexing to explain the histogenesis of the present testicular tumor that displayed the morphologic and immunophenotypic features of myoepithelioma.

Morphologically, myoepithelial differentiation in tumors may be difficult to evaluate only on the routine hematoxylin and eosin stained slides due to the variable morphological appearance of myoepithelial cells, and performing immunohistochemical stains is necessary to reach the correct diagnosis. Although salivary gland myoepitheliomas are well established, myoepitheliomas of other locations have been more recently recognized. Perhaps the greatest impediment to their recognition at sites other than salivary glands is the plasticity of myoepithelial cells and the resultant broad morphologic spectrum of myoepithelial tumors.³ Myoepitheliomas in the salivary glands are generally positive for pancytokeratin as well as myoepithelial markers (calponin, S-100, GFAP, α -SMA, cytokeratin 14, and p63), but the frequency of positivity and the percentage of positive cells with the individual markers are highly variable. S-100 protein has been reported to be the most useful marker, but it also lacks specificity.¹⁴ As to the immunohistochemical profile of the tumor described herein, the proliferating cells were focally strong positive for pancytokeratin and S-100 protein, but α -SMA labeling, which is an established myoepithelial marker, could not be detected. The typical immunophenotypes of pure myoepithelioma in salivary gland are known to express vimentin and

S-100 protein rather than actin or basal cytokeratin.^{14,15} In the series of soft tissue myoepitheliomas by Hornick and Fletcher,³ 93% of the tumors were positive for keratin and 63% of the tumor were positive for EMA. Immunoreactivity for S-100 protein was present in 87% of the tumor. The positivity for the other markers was variable. Thus, in addition to the morphological changes akin to myoepithelioma, the immunophenotypic expression toward myoepithelial differentiation suggests that the present tumor could be recognized as being myoepithelial in nature.

The criteria that have been reported to be helpful in differentiating between benign and malignant myoepitheliomas in the salivary glands include cytologic atypia, increased mitotic activity, and tumor infiltration into the surrounding tissue.¹⁶ In contrast to their salivary gland counterparts, myoepithelial carcinomas of soft tissue are distinguished from benign myoepitheliomas on the basis of the cytologic feature rather than the architectural features. Nearly half of the cases in the series of Hornick and Fletcher³ showed a microscopically infiltrative margin and this feature was associated with neither recurrence nor metastasis. In the present case, there was no evidence of an infiltrative margin, significant cytologic atypia and increased mitoses. Therefore, we consider this tumor was a benign tumor.

Testicular stromal tumors account for 3% to 4% of all testicular tumors. Most are pure Leydig cell tumors and the remainder show variable combinations of Sertoli cells, Leydig cells, granulosa-theca cells and undifferentiated gonadal stromal cells.¹² Testicular sex cord-stromal tumors with varying degrees of Sertoli or granulosa cell differentiation may also exhibit evidence of both epithelial and mesenchymal differentiation, but these tumors characteristically express inhibin- α .¹⁷ The present case did not show any immunoreactivity for inhibin- α , and the tumor did not follow the well-known histology of gonadal sex cord stromal tumor.

Tumors should be classified on the basis of what they in fact are, as defined by a series of appropriate phenotypic differentiation markers, rather than on the basis of equivocal assumptions about their origins.¹⁸ In other words, the morphologic feature of any tumor may be reflect a pattern of gene expression during oncogenesis rather than their origin from a specific cell lineage. So, it is appropriate that this testicular stromal tumor is named as 'myoepithelioma,' although its histogenesis remains a mystery.

REFERENCES

1. Hikino H, Nagaoka S, Miura H, Kurosumi M. Benign myoepithelioma of the breast: origin and development. *Pathol Int* 2009; 59: 422-6.
2. Kutzner H, Mentzel T, Kaddu S, Soares LM, Sanguenza OP, Requena L. Cutaneous myoepithelioma: an under-recognized cutaneous neoplasm composed of myoepithelial cells. *Am J Surg Pathol* 2001; 25: 348-55.
3. Hornick JL, Fletcher CD. Myoepithelial tumors of soft tissue: a clinicopathologic and immunohistochemical study of 101 cases with evaluation of prognostic parameters. *Am J Surg Pathol* 2003; 27: 1183-96.
4. Ellis GL, Auclair PL. Tumors of salivary glands. Atlas of tumor pathology, 3rd series, fascicle 17. Washington, DC: Armed Forces Institute of Pathology, 1996; 57.
5. Dardick I, Thomas MJ, van Nostrand AW. Myoepithelioma: new concepts of histology and classification: a light and electron microscopic study. *Ultrastruct Pathol* 1989; 13: 187-224.
6. Dardick I, Cavell S, Boivin M, *et al.* Salivary gland myoepithelioma variants: histological, ultrastructural, and immunocytological features. *Virchows Arch A Pathol Anat Histopathol* 1989; 416: 25-42.
7. Dardick I. Myoepithelioma: definitions and diagnostic criteria. *Ultrastruct Pathol* 1995; 19: 335-45.
8. Barnes L, Appel BN, Perez H, El-Attar AM. Myoepithelioma of the head and neck: case report and review. *J Surg Oncol* 1985; 28: 21-8.
9. Hamperl H. The myoepithelia (myoepithelial cells). Normal state; regressive changes; hyperplasia; tumors. *Curr Top Pathol* 1970; 53: 161-220.
10. Vilar O, Paulsen CA, Moore DJ. Electron microscopy of the human seminiferous tubules. *Adv Exp Med Biol* 1970; 10: 63-70.
11. Kuroda N, Nakayama H, Miyazaki E, *et al.* Distribution and role of CD34-positive stromal cells and myofibroblasts in human normal testicular stroma. *Histol Histopathol* 2004; 19: 743-51.
12. Weidner N. Myoid gonadal stromal tumor with epithelial differentiation (? testicular myoepithelioma). *Ultrastruct Pathol* 1991; 15: 409-16.
13. Miettinen M, Salo J, Virtanen I. Testicular stromal tumor: ultrastructural, immunohistochemical, and gel electrophoretic evidence of epithelial differentiation. *Ultrastruct Pathol* 1986; 10: 515-28.
14. Simpson RH, Jones H, Beasley P. Benign myoepithelioma of the salivary glands: a true entity? *Histopathology* 1995; 27: 1-9.
15. Seifert G. Are adenomyoepithelioma of the breast and epithelial-myoepithelial carcinoma of the salivary glands identical tumours? *Virchows Arch* 1998; 433: 285-8.
16. Nagao T, Sugano I, Ishida Y, *et al.* Salivary gland malignant myoepithelioma: a clinicopathologic and immunohistochemical study of ten cases. *Cancer* 1998; 83: 1292-9.
17. McCluggage WG, Shanks JH, Whiteside C, Maxwell P, Banerjee SS, Biggart JD. Immunohistochemical study of testicular sex cord-stromal tumors, including staining with anti-inhibin antibody. *Am J Surg Pathol* 1998; 22: 615-9.
18. Gould VE. Histogenesis and differentiation: a re-evaluation of these concepts as criteria for the classification of tumors. *Hum Pathol* 1986; 17: 212-5.